SYNOPSIS

STUDY OF EFFECT OF SELECTED NON STEROIDAL ANTI-INFLAMMATORY DRUGS (PIROXICAM AND NIMESULIDE) ON SWORDTAIL FISH, XIPHOPHORUS HELLERI (Heckel, 1848)

Introduction

The thirst of human society for technological development and growth is invariably leading to alarming rate of consumption of natural resources and tainting of aquatic environment by their waste and byproducts. The world has seen an improvement in human health support system. This has gone hand-in-hand with the consorting of health system and the drug manufacturers leading to indiscriminate prescription and sale of drugs over the counter. There has been a steady increase in consumption of medicinal drugs and antifungal drugs alike. A rapidly growing body of scientific and research documentation indicates that a number of substances have the potential to interfere with normal functions of the body in animals.

Antifungal substances in our surroundings, food, consumer products which interfere with different physiological processes and the normal homeostasis of vital processes are becoming more and more of concern.

There is ever increasing evidence which clearly indicates that antifungal drugs have affects on general metabolism. Results from animal experimentation, clinical observations in human and other sources implicate antifungals as a significant concern to environmental and human health.

Research both at national and international level has involved observation and experimentation on many different animal models. Most of the research so far has been done on mammals, especially rodent, owing to the possibility of direct correlation of such studies with higher mammals. But in the interest of conservation of animal biodiversity more research in non-mammalian animal models is also necessary to enrich our understanding of the impact of these chemicals on the different non-mammalian organisms in the environment.

Review of literature and development in the subject

(previous work done in the relevant area):

Many biologists have studied the different aspects of biology and physiology of fresh water fish (Murdy, 1997; Zhang, 2008; Cleuvers, 2003; Lee, 2011; Schwaiger, 2004; Mehinto, 2010; Avdeef, 1998; Hayashi, 2008; Kasprazyl-Hordern, 2008; Kim, 2007; Christensen, 2009; Flippin, 2007; Haeckman, 2008). Yet there are so many species of fish and environment and fish interactions about which there is a lack of understanding and clarity. Such grey areas in our knowledge need to be studied in more detail.

Objectives Of Research/ Proposed Hypothesis

There are gaps in our knowledge of the methodologies for analysis, exposures and effects of the NSAIDs. Therefore, new information and activities relevant to these drugs are being developed rapidly. This effort calls for effective coordination of research, testing, assessment and management.

Research would be needed in a number of fields to enable us obtain insight into the affects of NSAIDs on natural populations of animals and to develop and validate novel whole organism assays for endocrine-disruption in non-mammalian vertebrates like fish, amphibians, reptiles and birds. These approaches would let us assess hazards to those species and to evaluate long term environmental effects.

On site field investigations are needed in the context of NSAID effects. These investigations should involve a broad based screen including assessment of gonadal function, behavioral patterns and offspring sex ratio, population size survival rate. Generally, environmental toxicity studies should focus on aquatic organisms as environmental exposure to industrial chemicals generally involves discharges to sewage. It is exposure assessment studies like this one that provide with the toxicity data required for conservation of organisms likely to be exposed and management of the chemicals involved.

About *Xiphophorus helleri* (Heckel, 1848)

Xiphophorus helleri is a fish found mainly in rapidly flowing streams and rivers, preferring heavily vegetated habitats. They occur in warm springs and their effluents, weedy canals and ponds. They feed on worms, crustaceans, insects and plant matter; and are used for genetics research. Especially the red varieties are very popular aquarium fishes.

This species is distributed across North and Central America in Rio Nantla, Veracruz in Mexico to northwestern Honduras; Africa: Feral populations reported from Natal and eastern Transvaal as well as in Lake Otjikoto, Namibia. Several countries report adverse ecological impact after introduction.

The present work proposes to study the effects of aquatic contaminants- NSAIDs- Piroxicam & Nimesulide on general biology of *Xiphophorus helleri*.

About Piroxicam

Piroxicam is a nonsteroidal anti-inflammatory drug (NSAID) of the oxicam class used to relieve the symptoms of painful inflammatory conditions like arthritis. Piroxicam works by preventing the production of endogenous prostaglandins which are involved in the mediation of pain, stiffness, tenderness and swelling. It is used in the treatment of rheumatoid and osteoarthritis, primary dysmenorrhoea, postoperative pain; and act as an analgesic, especially where there is inflammation.

Similar to other NSAIDs the principal side effects of piroxicam administration include: digestive complaints like nausea, discomfort, diarrhoea and bleeds or ulceration of the stomach, as well as headache, dizziness, nervousness, depression, drowsiness, insomnia, vertigo, hearing disturbances (such as tinnitus), high blood pressure, oedema, light sensitivity, skin reactions.

Residues of NSAIDs are currently being detected in surface waters and aquatic organisms throughout the UK and Europe. However, the levels of these residues in fish and other aquatic organisms, particularly lower trophic level prey species, have not yet been determined. While exposure to diclofenac is known to adversely affect fish, the degree to which other aquatic organisms are exposed and impacted through continuous ingestion of contaminated prey and interaction with the aquatic habitat remains unknown. The extent and effects of exposure to ibuprofen also remain largely unknown (Richards et al., 2011).

Pharmaceuticals are becoming widely distributed in waters and wastewaters and pose a serious threat to public health. The present study aimed to analyze non-steroidal anti-inflammatory drugs (NSAIDs) in surface waters, drinking water, and wastewater in Tehran, Iran. Results of this study showed that the measured pharmaceuticals were detected in all rivers with low concentrations in nanograms per liter range. Furthermore,

this study showed that the aforementioned pharmaceuticals are not completely removed during their passage through waste water treatment plants (Eslami et al., 2015).

About Nimesulide

Nimesulide is a nonsteroidal antiinflammatory drug (NSAID) with relative specificity for COX-2 that is not available in the United States, but is used widely in other countries in the treatment of acute pain. Nimesulide has been linked to many instances of clinical acute liver injury that can be severe and can result in acute liver failure and even death. There have been several reports of adverse drug reactions in India. On February 12, 2011, Indian Express reported that the Union Ministry of Health and Family Welfare finally decided to suspend the pediatric use of this drug. From 10 March 2011 onward Nimesulide formulations are not allowed for human use in children below 12 years of age.

The anti-inflammatory, analgesic and antipyretic activities of nimesulide, a non-steroidal anti-inflammatory drug (NSAID) of the sulfonanilide class, have been demonstrated in a number of experimental models and in numerous clinical trials. Nimesulide has exhibited potency similar to or greater than that of indomethacin, diclofenac, piroxicam and ibuprofen in standard animal models of inflammation such as carrageenin-induced rat paw oedema and inflammation, ultraviolet light-induced erythema in guinea-pigs and adjuvant arthritis in rats. The analgesic potency of nimesulide was similar to that of ibuprofen and less than that of indomethacin in an acetic acid writhing test in rats, and acetic acid and acetylcholine writhing tests in mice. Nimesulide has shown superior antipyretic potency to indomethacin, ibuprofen, aspirin and paracetamol (acetaminophen) in rats with yeast-induced fever (Davis & Brogden, 1994).

There is a widespread occurrence of many NSAIDs, including Nimesulide, in aqueous environments and its potential for ecological impact has been of growing concern (Christensen et al., 2009). Nimesulide, like other NSAIDs, is known to influence cyclo-oxygenase (COX) pathway (Flippin et al., 2007; Haeckmann et al., 2008). Therefore Nimesulide contamination could affect reproduction of aquatic animals. It

is used relieve mild to moderate pain (including pain after surgery), dental pain, headache and pain from kidney stone.

Methodology to be adopted

Determination of Total Fecundity would be done made by closely monitoring litter size of each breeding female selected for experimentation. Parallely, analysis of secondary sexual characters like coloration, mating behavior would be done. The above experiments would be performed at different exposure times to the selected chemicals and their effects evaluated in the context of environmental and reproductive health of the fish.

The biochemical analysis of tissue (protein, carbohydrate and lipids) will be done by different standard estimation methods.

Study of respiratory parameter, rate of oxygen consumption and total oxygen consumption would be carried out by the standard Winkler's Method.

Importance Of Study / Society Application

Xiphophorus helleri is a fish found mainly in rapidly flowing streams and rivers, preferring heavily vegetated habitats. They occur in warm springs and their effluents, weedy canals and ponds. They feed on worms, crustaceans, insects and plant matter; and are used for genetics research. Especially the red varieties are very popular aquarium fishes.

The study on biological aspects will become helpful because of the relevance to direct extrapolation to other lower and higher vertebrates. The sword tail fish is having good demand as an experimental model for genetic studies. The breeding and farming of this fish has potential as an enterprise. Fish have great significance in the life mankind, being an important natural source of protein and providing certain other useful products as well as economic sustenance to many nations.

Proposed Work plan/Formulation and structure of study

Year Wise Plan Of Research Work

First year:- Review of literature, collection of references, material and methods, collection of samples will be done.

Second year:- Collection and preservation of samples, processing of samples, preparation of histological slides and biochemical analysis of tissues.

Third Year:- Analysis of statistical data, documentation and presentation of data, calculations, results, discussions, conclusion and summary. Preparation of synopsis and draft of thesis.

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